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(54) Title: **COMPLEMENTING CELL LINES**

(57) Abstract: A packaging cell line capable of complementing recombinant adenoviruses based on serotypes from subgroup B, preferably adenovirus type 35. The cell line is preferably derived from primary, diploid human cells (e.g., primary human retinoblasts, primary human embryonic kidney cells and primary human amniocytes) which are transformed by adenovirus E1 sequences. Also disclosed is a cell line derived from PER.C6 (ECACC deposit number 96022940), which cell expresses functional Ad35 E1B sequences. The new cell lines are useful for producing recombinant adenoviruses designed for gene therapy and vaccination. The cell lines can also be used for producing human recombinant therapeutic proteins. In addition, the cell lines are useful for producing human viruses other than adenovirus such as influenza virus, herpes simplex virus, rotavirus, measles virus.

# INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12N15/10 C12N15/86 C12N7/01 C12N7/02

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 199 18 023 A (CICHON GUENTER) 21 September 2000 (2000-09-21)  the whole document	1-17, 19-21, 33-42
X	WO 99 32647 A (INTROGENE BV ;SCHOUTEN GOVERT (NL); EINERHAND MARCUS PETER WILHELM) 1 July 1999 (1999-07-01) abstract page 3, line 14 -page 7, line 23 page 21, line 10 - line 13	1-17,19, 20,33-42
X	DE 197 54 103 A (HEPAVEC AG FUER GENTHERAPIE) 10 June 1999 (1999-06-10)  the whole document	1-17, 19-21, 33-42

☒ Further documents are listed in the continuation of box C.

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 198 07 265 A (CENTEON PHARMA GMBH) 26 August 1999 (1999-08-26) abstract column 4, line 16 - line 37 ---	1-17, 19, 20, 33-42
X	WO 98 17783 A (UNIV MICHIGAN) 30 April 1998 (1998-04-30) the whole document ---	1, 3, 5-11
A		2, 4, 12-42
X	WO 97 00326 A (FALLAUX FRITS JACOBUS ; UNIV LEIDEN (NL); BOUT ABRAHAM (NL); EB ALE) 3 January 1997 (1997-01-03) abstract page 3, line 16 - line 24 page 10, line 29 - page 11, line 14 page 18, line 25 - page 19, line 19 examples claims ---	1-17, 19, 20, 33-42
A	US 5 880 102 A (BLAZING MICHAEL A ET AL) 9 March 1999 (1999-03-09) abstract examples ---	1-42
X	SCHIEDNER G ET AL: "EFFICIENT TRANSFORMATION OF PRIMARY HUMAN AMNIOCYTES BY E1 FUNCTIONS OF AD5: GENERATION OF NEW CELL LINES FOR ADENOVIRAL VECTOR PRODUCTION" HUMAN GENE THERAPY, XX, XX, vol. 11, no. 15, 10 October 2000 (2000-10-10), pages 2105-2116, XP000974022 ISSN: 1043-0342 the whole document ---	1-17, 19-21, 33-42
A	RUMPF H ET AL: "Two domains within the adenovirus type 12 E1A unique spacer have disparate effects on the interaction of E1A with P105- Rb and the transformation of primary mouse cells" VIROLOGY, ACADEMIC PRESS, ORLANDO, US, vol. 257, no. 1, 25 April 1999 (1999-04-25), pages 45-53, XP002134555 ISSN: 0042-6822 the whole document -----	1-42

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International Application No  
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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
DE 19918023	A	21-09-2000	DE 19918023 A1	21-09-2000
✓ WO 9932647	A	01-07-1999	AU 1787499 A	12-07-1999
			CA 2316414 A1	01-07-1999
			EP 1042494 A1	11-10-2000
			JP 2001526900 T	25-12-2001
			WO 9932647 A1	01-07-1999
DE 19754103	A	10-06-1999	DE 19754103 A1	10-06-1999
DE 19807265	A	26-08-1999	DE 19807265 A1	26-08-1999
			AU 1737899 A	02-09-1999
			EP 0950713 A2	20-10-1999
			JP 11285394 A	19-10-1999
WO 9817783	A	30-04-1998	US 5994132 A	30-11-1999
			AU 5152998 A	15-05-1998
			EP 0935648 A1	18-08-1999
			WO 9817783 A1	30-04-1998
			US 6063622 A	16-05-2000
			US 6083750 A	04-07-2000
			US 6057158 A	02-05-2000
✓ WO 9700326	A	03-01-1997	AU 731767 B2	05-04-2001
			AU 6018296 A	15-01-1997
			CA 2222140 A1	03-01-1997
			EP 0833934 A1	08-04-1998
			JP 11507552 T	06-07-1999
			WO 9700326 A1	03-01-1997
			US 6395519 B1	28-05-2002
			US 6306652 B1	23-10-2001
			US 6238893 B1	29-05-2001
			US 6265212 B1	24-07-2001
			US 5994128 A	30-11-1999
			US 6033908 A	07-03-2000
US 5880102	A	09-03-1999	NONE	